

ATGCCCTGCGTGCAAGCCCAGTATAGCCCTTCACCTCCGGGGTCCACTTACGCCACGCAG
 ACTTATGGCTCGGAATACACCACAGAAATCATGAACCCCGACTACACCAAGCTGACCATG
 GACCTCGGTAGCACGGGGATCATGGCCACCGCCACTACATCCCTGCCAGCTTCAGTACC
 TTCATGGAGGGCTACCCAGCAGCTGCGAACTCAAGCCCTCCTGCCGTGTACCAAATGCCG
 CTTTCTGGGCCTCGGCCTTTGATCAAGATGGAAGAGGGTCGCGAGCATGGCTACCACCAC
 CACCATCACCATCACCATCATCACCACCACCACCAGCAACAGCAGCCGTCCATTCCCTCCT
 CCCTCCGGCCCCGAGGACGAGGTACTGCCCAGCACCTCCATGTACTTCAAGCAGTCTCCG
 CCGTCTACACCGACCACTCCAGGCTTCCCCCGCAGGCGGGGGCGCTGTGGGACGACGAG
 CTGCCCTCTGCGCCTGGCTGCATCGCTCCGGGACCGCTGCTGGACCCGCAGATGAAGGCG
 GTACCCCCCATGGCCGCTGCTGCGCGCTTCCCGATCTTCTTCAAGCCCTCACCAGCCACAC
 CCTCCCGCGCCAGTCCAGCCGGCGGCCACCACCTCGGCTATGACCCACGGCCGCAGCT
 GCACTCAGTCTGCCCCCTGGGAGCCGCGGCCGAGCAGGCAGCCAAGCTGCTGCGCTCGAG
 GGCCACCCATACGGGCTCCCGCTGGCCAAGAGGACGGCCACGCTGACCTTCCCTCCGCTG
 GGCCTCACAGCCTCCCCACCGCGTCCAGCCTGCTGGGAGAGAGCCCCAGCCTCCCATCG
 CCACCCAATAGGAGCTCATCATCTGGGGAAGGCACATGTGCCGTGTGCGGCGACAACGCT
 GCCTGCCAGCACTACGGAGTCCGCACCTGCGAGGGCTGCAAGGGCTTCTTCAAGAGAACG
 GTGCAGAAAAATGCAAAATATGTTTGCTGGCAAATAAAAACTGCCAGTGGACAAGAGA
 CGCCGAAACCGATGTCTAGTACTGCAGATTTTCAAGTGTCTCAGTGTGCGGATGGTTAAG
 GAAGTTGTGCGTACAGACAGTCTGAAAGGGAGGAGAGGTCGTCTGCCCTTCCAAACCAAAG
 AGCCCACTACAACAGGAGCCCTCGCAGCCCTCCCCGCCATCTCCTCCGATCTGTATGATG
 AATGCCCTTGTCCGAGCTTTAACAGATGCAACACCCAGAGATCTTGATTATTCCAGATAC
 TGTCCCACCGACCAAGGCCACTGCAGGCACAGATGCTGAGCACGTGCAACAGTTCTACAAC
 CTTCTGACGGCCTCCATTGACGTGTCCAGAAGCTGGGCAGAAAAGATCCCAGGATTCACCT
 GATCTCCCCAAAGAAGATCAGACGTTACTTATAGAATCAGCCTTTTTGGAGCTGTTGTT
 CTTAGACTTTCCATCAGGTCAAACACTGCTGAAGATAAGTTTGTGTTCTGCAATGCACTT
 GTCTGTCATCGACTTCAGTGCCTTCGAGGATTTGGGGAGTGGCTCGACTCCATTAAAGAC
 TTTTCTTTTAACTTGCAGAGCCTGAACCTTGATATCCAAGCCTTAGCCTGCCTGTCAGCA
 CTGAGTATGATCACAGAGCGACATGGGTAAAAAGAACCAAGAGAGTGGAGGAGCTATGC
 ACCAAGATCACAGCAGCTTAAAGGACCACCAGAGGAAGGGACAGGCTCTGGAGCCCTCG
 GAGCCTAAGGTCTGCGCGCGCTGGTAGAACTGAGAAAGATCTGTACCCAGGGCCTCCAG
 CGCATCTTCTACCTGAAGCTAGAGGACTTGGTACCTCCACCTTCTGTCATCGACAAGCTC
 TTCCTTGACACCCTGCCTTTCTGA (SEQ ID NO:1)

MPCVQAQYSPSPPGSTYATQTYGSEYTTEIMNPDYTKLTMDLGS
 TGIMATATTSLPSTFMEGYPSSELKPSCLYQMPPSGPRPLIKMEEGREHGYHHHH
 HHHHHHHHHQQQPSIPPPSGPEDEVLPSTSMYFKQSPSTPTTPGFPPQAGALWDE
 LPSAPGCIAPGPLLDPMKAVPPMAAAARFPIFFKPSPPHPPAPSPAGGHHLGYDPTA
 AAALSLPLGAAAAAGSQAALLEGHPYGLPLAKRTATLTFPPLGLTASPTASSLLGESP
 SLPSPPNRSSSSGEGTCAVCGDNAACQHYGVRTCEGCKGFFKRTVQKNKYVCLANKN
 CPVDKRRRNRCQYCRFQKCLSVGMVKEVVRTDSLKGRRRLPSKPKSPLQQEPSQSP
 PSPPICMMNALVRALTDATPRDLDSRYCPTDQATAGTDAEHVQQFYNNLLTASIDVSR
 SWAEKIPGFTDLPKEDQTLLESFALELFVLRSLRSNTAEDKFVFCNGLVLHRLQCL
 RGFGEWLDISKDFSLNLQSLNLDIQALACLSALSMITERHGLKEPKRVEELCTKITSS
 LKDHRKQGALEPSEPKVLRALVELRKICTQGLQRIFYLKLEDLVPPPSVIDKLFLDT
 LPF (SEQ ID NO:2)

FIGURE 1

1 ccgagtctcc tgcctcccgc cccccacccc tccagcgccct gctcctcctc cgctccccat
 61 acacagacac gctcacaccc gctccttcac ttgcacacac agacacacgc gcgctcacac
 121 gctcgcgaca cacactccac tctctcccgc gcgctcacac ccctctctct cgcgccctc
 181 gccggtgtcg cgccgcgcgc cgccgcagcc ggacgcccct ccagggtca ctttgcaacg
 241 ctgacagagc gggcagtggc cgtggagggtg ggaaacgtgg cgacatccta gcccctggtc
 301 gcagccggag actggacgct gcggaacctc tcggcggcgc tctcccatga gttgggatcg
 361 cagcatcccc agccagcgcg tgctcacgcg ctctgggagc cgctgggttt gtgcaccgca
 421 gcccttccgc gacagcagct gtgactctcc cccaatccag atttcggggt cgctctctag
 481 aaactcgctc taaagacgga acctccacag aacccaaagc ccactgcggg agagcgagc
 541 ccgacaagcc cgggcgctga gcctggaccc tcaacagagc gggccagcac agcggcggcg
 601 gctgcttcgc ctatcccgcg gtccccgcct cctacactct cagcctccgc tggagagacc
 661 cccagcccca ccattcagcg cgcaagatac cctccagata tgccctgcgt gcaagcccaa
 721 tatagccctt cgcctccggg gtccacttat gccacgcaga cttatggctc ggaatacacc
 781 acagaaatca tgaaccccga ctatgccaag ctgacctagg acctcggtag cacggggatc
 841 atggccacgg ccacgacgct cctgcccagc ttcagtacct tcatggaggg ctaccccagc
 901 agctgcgaac tcaagccctc ctgctgttac caaatgccgc cttctgggcc tcggcctttg
 961 atcaagatgg aagagggtcg cgagcatggc taccaccacc accaccacca tcaccatcat
 1021 catcaccacc accaccagca gcagcagccg tccattcctc ctccctctgg ccccgaggac
 1081 gaggtactgc ccagcacctc catgtacttc aagcagtcct cgccgtctac gccgacct
 1141 ccaggcttcc ccccgagcgc gggggcgctg tgggacgacg agctgccctc tgcgcctggc
 1201 tgcacgctc cgggaccgct gctggaccgc cagatgaagg cagtgcctcc aatggccgct
 1261 gctgcgcgct tcccgatctt cttaagccc tcaccgccac accctccgc gccagccca
 1321 gccggcgccc accacctggg ctatgacccc acggccgcag ctgcgctcag tctaccctg
 1381 ggagccgcgc cgccgcgcgc cagccaagct gctgcgctcg agggccatcc gtacgggctc
 1441 ccgctggcca agaggacggc cagcttgacc ttcctccgc tgggcctcac agcgtcccct
 1501 accgcgtcca gcctgctggg agagagcccc agcctaccat cgccacccaa taggagctca
 1561 tcatccggcg agggcacgtg tgctgtgtgc ggggacaatg ctgcctgcca gcactacgga
 1621 gtccgcacct gcgagggtcg caagggttc ttcaagagaa cgggtgcagaa aaacgcaaaa
 1681 tatgtttgct tggcaataaa aaactgcccg gtagacaaga gacgtcgaaa tcgatgtcag
 1741 tactgcaggt ttcagaagtg tctcagtgtc gggatggtga aggaagtgtg gcgtacagat
 1801 agtctgaaag ggaggagagg tcgtctgcct tccaaaccaa agagcccact acaacaggag
 1861 cctcgcagc cctcccacc atctcctccg atctgtatga tgaacgcctc tgcgcagct
 1921 ttaacagacg caacgcccag agaccttgat tactccagat actgtcccac cgaccaggcc
 1981 actgcccggc cagacgctga gcacgtgcag cagttctaca acctctgac ggcctccatc
 2041 gacgtgtcca gaagctgggc agaaaagatc cccggattca ctgatctccc caaagaagat
 2101 cagacgttac ttatagaatc agcctttttg gagctgttcg ttcttagact ttctatcagg
 2161 tcaaactctg ctgaagataa gtttgtgttc tgcaatggac ttgtcctgca ccgacttcag
 2221 tgccttcgcg gatttgggga gtggctcgac tccattaaag acttttcttt aaatttgcag
 2281 agcctgaacc ttgatatcca agccttagcc tgccgtgcag cactgagtat gatcacagag
 2341 cgacatgggt taaaagaacc aaagagagtg gaggagctat gcaacaagat cacaagcagc
 2401 ttaaaggacc accagaggaa gggacaggct ctggagccct cagagcccaa ggtccttcgc
 2461 gactggtgg aactgaggaa gatctgcacc cagggcctcc agcgtatctt ctacctgaag
 2521 ctggaggact tgggtgcccc acctctgtc atcgacaagc tcttccttga taccctgcct
 2581 ttctgagcag gggaagcctg agcagagagc tacttgctct gctggcactg gtcattaaag
 2641 gagcaaaagg atgggtttga acacctgccc ctctatcctt cctccagggg aaaaagcagc
 2701 tcccatagaa agcaaagact tttttttttc ctggcacctt tccttacaac ctaaagccag
 2761 aaaccttgca gagtattgtg ttgggttgtt gttttatatt taggctttgg tgggtgggct
 2821 gggagggggt aaaatagttc atgaggcttt tctaagaaat tgctgacgaa gcacttttgg
 2881 atgatgctat cccagcagtg ggggtggggag aaaggataat ataactgttt taaaaactct
 2941 ttccggggga atatgactat ggttgccttg tatttaaaaa taagaacagc caagggtgtg
 3001 tttaccaggg tagggctgtg tcttaagact gatcccttta gtatgtactt cccgagtcga
 3061 ggcacataag tggtgcaaat gaggcgggga aattcttcat ttcttcattt ctttctctt
 3121 cttaaaataa aatggcaaaa aaaaaagat ggaagattat ctacaaatca gacttagcaa

FIGURE 2A

3181 aatgataatg gctattcgtc tccacataca agtgcaattt tttagagtgc tgtcttacta
 3241 agtccttggtt gtgaactctc cctcatttta tatgaaaata agaaggaggc agtcagtgtta
 3301 tcaaacggcg tgctcatttt cctagctcac ccttggtcca cctgccctgt agaacccttc
 3361 ggagggtatg cccttctaag actttcaggc cactcttgat ggaattcgac acccctcccc
 3421 tcaaccctatg actatccaga tgcctgaat ggggatcagg ttataaaatg gattgcatat
 3481 gactgtgttc gctgtgtgtt tgtcaacctg gacagagttc tctaaacctt ctttagttgt
 3541 agcaagttcc tgattcctcc attcagaagc ccaaggagca ttgggtgact cgatcaaggg
 3601 ttaaccctag gagaacatgc aaataagtag gaactgggtc agacagggtta agcaccagag
 3661 atgataagga tttatatata aatatatata aaattaattt ttgttattgg ttatagacaa
 3721 ttttggaag caagagaatc atctcttttt tttttttaa gaggaaga tagtattgat
 3781 gtattagcaa agattagtgg ggtacgggtc aacattccgt gtttggtgccc ctttttctat
 3841 gtttctactg ttgatggcat attattatga aatgattcgt tgcatagtgt cttattttgt
 3901 atgaacattt gtatgcacgt tctattgtaa tcgctttgcc tgtatttatt gcaagaccac
 3961 cagctcctgg aggctgagtt acagaataat caaatggggt gttcgtgggtg acttggatac
 4021 accggttaga aattaaataa gcatatatat atatataaaa acatagcagg ttacatatat
 4081 atttataatg tgtcttttta ttaaccattt gtacaataaa tgtcacttcc cagcagtta
 4141 ttttatcctt tgtttgcatg gacctttaag gcagcactgt ttagcacttt gatatgaaat
 4201 tttttgctta ttttttgct aaattcaa aacgtttgaa gatttttagg tctaaaagtc
 4261 tttatattat atacactgta tcaagtcaag atacctttgg ccgttttgct aagactcaaa
 4321 ctttgaatgt caaaccaatg tcacggtagc ttctgttagc ttttaatcat ttttgcttta
 4381 gtcttttttt ttaaaaaaaa (SEQ ID NO:3)

MPCVQAQYSPSPPGSTYATQTYGSEYTTTEIMNPDYAKLTMDLGSTGIMATATTSLSFSTFMEGYPSSCELKPSCLYQMPPSGPRP
 LIKMEEGREHGYHHHHHHHHHHHHHHQQQQPSIPPPSGPEDEVLPTSMYFKQSPSTPTTPGFPPQAGALWDELPSAPGCIAPG
 PLLDPQMKAVPPMAAAARFPIFFKPSPPHPPAPSPAGGHLGYDPTAAAALSLPLGAAAAAGSQAAALEGHPYGLPLAKRTATLTF
 PPLGLTASPTASSLLGESPSLSPPNRSSSSGEGTCAVCGDNAACQHYGVRTCEGCKGFFKRTVQKNKYVCLANKNCPVDKRRRN
 RCQYCRFQKCLSVGMVKEVVRTDSLKGRRGRRLPSKPKSPLQQEPSQSPSPPICMNNALVRALTDATPRDLDSRYCPTDQATAG
 TDAEHVQQFYNLLTASIDVSRSWAEKIPGFTDLPKEDQTLLESFAFLEFLVRLSIRSNTAEDKFVFCNGLVLHRLQLRGFGWL
 DSIKDFSLNLQSLNLDIQAACLSALSMITERHGLKEPKRVEELCNKITSSLKDHQRKGQALEPSEPKVLRALVELRKICTQGLQR
 IFYKLLEDLVSPPSVIDKFLDLTLPF (SEQ ID NO:4)

FIGURE 2B

underlined = deleted in targeting construct

[] = sequence flanking Neo insert in targeting construct

[ATGCCCTGCGTGCAAGC] CCAGTATAGCCCTTCACCTCCGGGGTCCACTTACGCCACGCAG
ACTTATGGCTCGGAATACACCACAGAAATCATGAACCCCGACTACACCAAGCTGACCATG
GACCTCGGTAGCACGGGGATCATGGCCACCGCCACTACATCCCTGCCCAGCTTCAGTACC
TTCATGGAGGGCTACCCCAGCAGCTGCGAACTCAAGCCCTCCTGCCTGTACCAAATGCCG
CCTTCTGGGCCTCGGC [CTTTGATCAAGATGGAAGAGGGTCGCGAGCATGGCTACCACCAC
CACCATCACCATCACCATCATCACCACCACCACCAGCAACAGCAGCCGTCCATTCTCTCT
CCCTCCGGCCCCGAGGACGAGGTACTGCCCAGCACCTCCATGTACTTCAAGCAGTCTCCG
CCGTCTACACCGACCACTCCAGGCTTCCCCCGCAGGCGGGGGCGCTGTGGGACGACGAG
CTGCCCTCTGCGCCTGGCTGCATCGCTCCGGGACCGCTGCTGGACCCGCAGATGAAGGCG
GTACCCCCCATGGCCGCTGCTGCGCGCTTCCCGATCTT] CTTCAAGCCCTCACCGCCACAC
CCTCCCGCGCCCCAGTCCAGCCGGCGGCCACCACCTCGGCTATGACCCACGGCCCGCAGCT
GCACTCAGTCTGCCCCGAGCCGCGGCCGAGCAGGCAGCCAAGCTGCTGCGCTCGAG
GGCCACCCATACGGGCTCCCGCTGGCCAAGAGGACGGCCACGCTGACCTTCCCTCCGCTG
GGCCTCACAGCCTCCCCACCGCTCCAGCCTGCTGGGAGAGAGCCCCAGCCTCCCATCG
CCACCCAATAGGAGCTCATCATCTGGGGAAGGCACATGTGCCGTGTGCGGCGACAACGCT
GCCTGCCAGCACTACGGAGTCCGCACCTGCGAGGGCTGCAAGGGCTTCTTCAAGAGAACG
GTGCAGAAAAATGCAAAATATGTTTGCCTGGCAAATAAAAACTGCCAGTGGACAAGAGA
CGCCGAAACCGATGTCAGTACTGCAGATTTCAAGAGTGTCTCAGTGTGCGGATGGTTAAG
GAAGTTGTGCGTACAGACAGTCTGAAAGGGAGGAGAGGTCTGCTTCCAAACCAAAG
AGCCCACTACAACAGGAGCCCTCGCAGCCCTCCCCGCCATCTCCTCCGATCTGTATGATG
AATGCCCTTGTCCGAGCTTTAACAGATGCAACACCCAGAGATCTTGATTATTCCAGATAC
TGTCCCACCGACCAAGGCCACTGCAGGCACAGATGCTGAGCACGTGCAACAGTTCTACAAC
CTTCTGACGGCCTCCATTGACGTGTCCAGAAGCTGGGCAGAAAAGATCCCAGGATTCACT
GATCTCCCCAAAGAAGATCAGACGTTACTTATAGAATCAGCCTTTTGGAGCTGTTTGT
CTTAGACTTTCCATCAGGTCAAACACTGCTGAAGATAAGTTTGTGTTCTGCAATGGACTT
GTCCTGCATCGACTTCAGTGCCTTCGAGGATTTGGGGAGTGGCTCGACTCCATTAAAGAC
TTTTCTTTAACTTGCAGAGCCTGAACCTTGATATCCAAGCCTTAGCCTGCCTGTCAGCA
CTGAGTATGATCACAGAGCGACATGGGTAAAAAGAACCAAGAGAGTGGAGGAGCTATGC
ACCAAGATCACAAGCAGCTTAAAGGACCACCAGAGGAAGGGACAGGCTCTGGAGCCCTCG
GAGCCTAAGGTCTGCGCGCGCTGGTAGAACTGAGAAAAGATCTGTACCCAGGGCCTCCAG
CGCATCTTCTACCTGAAGCTAGAGGACTTGGTACCTCCACCTTCTGTCTATGACAAGCTC
TTCCTTGACACCCTGCCTTTCTGA

FIGURE 3A

Gene Sequence Structure *

18 bp

Sequence Deleted

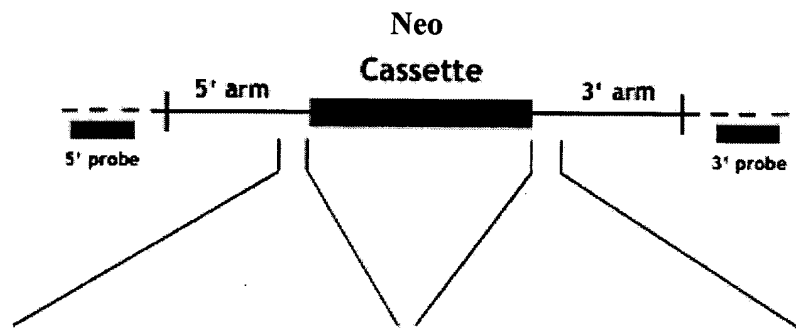
256 bp

Size of full-length
cDNA: 1884 bp

Targeting Vector*
(genomic sequence)

Construct Number: 4512

Arm Length:
5': 2.7 kb
3': 3 kb



———— Targeting Vector
----- Endogenous Locus

* Not drawn to scale

5' >CCCTTTGACAGTCAGGAACTC
AGCTGTCTTCCCAGCCAGGAAGAA
AGTAAGCTAGGAGCATTCACTCTT
TGCCAGCAGGTGGGAGAGGATACC
ACTTTCTTGTTTCTGATTCAAGA
GCAGTGGAACCAGCTGCAGATGGA
GTGTCAACTGGCTTCTGAGCCCTT
TTCTCTGTCCCTCCAGATATGCCC
TGCGTGCAAGC<3'
(SEQ ID NO:5)

5' >CTTTGATCAAGATGGAAGAGG
ATCGCGAGCATGGCTACCAACCACC
ACCATCACCATCACCATCATCACC
ACCACCACCAGCAACAGCAGCCGT
CCATTCTCCTCCCTCCGGCCCCG
AGGACGAGGTACTGCCCAGCACCT
CCATGTACTTCAAGCAGTCTCCGC
CGTCTACACCGACCACCCAGGCT
TCCCCCGCAG<3'
(SEQ ID NO:6)

FIGURE 3B

Rotarod

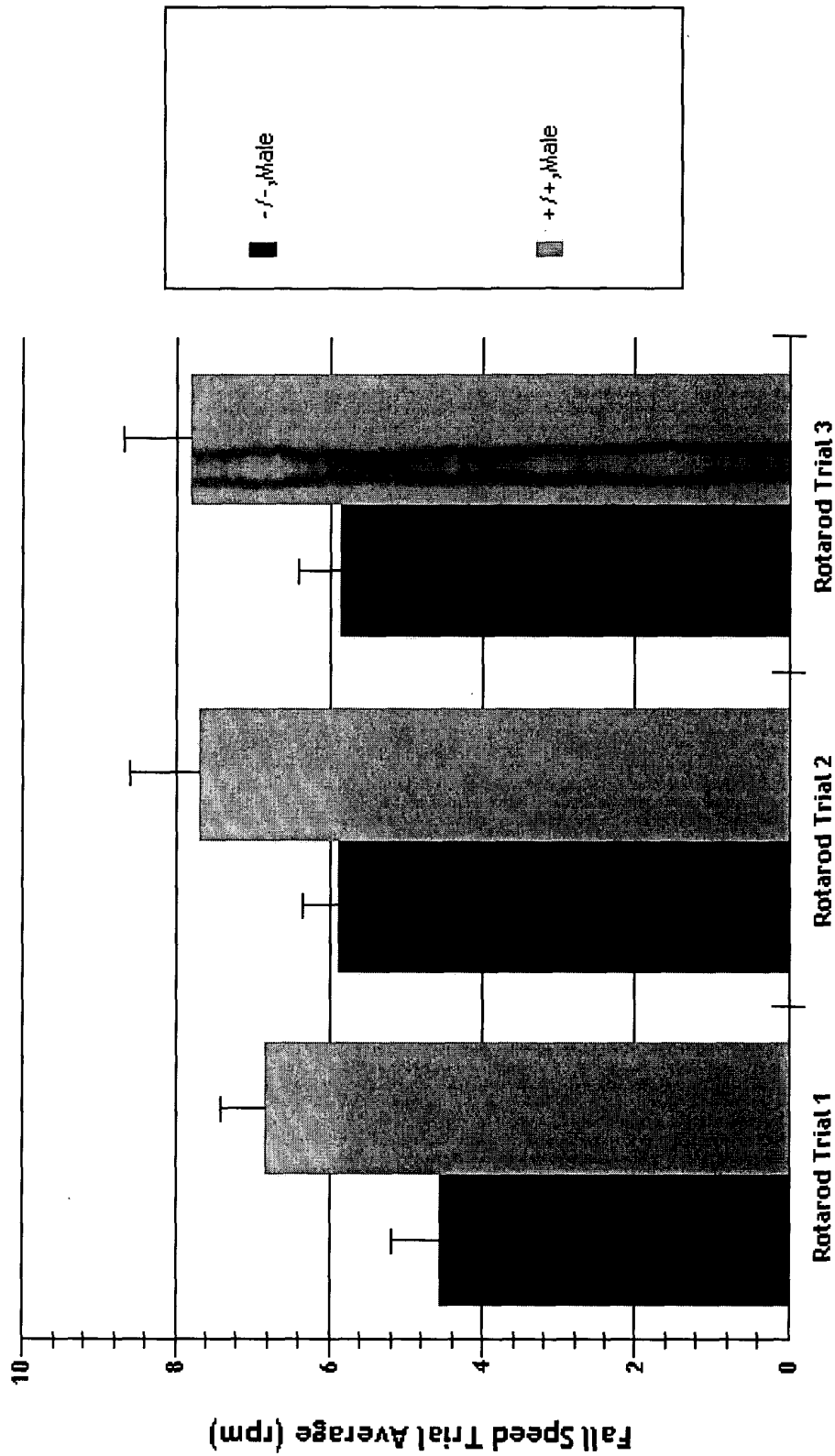


FIGURE 4

